

0989111313



FIG. 2

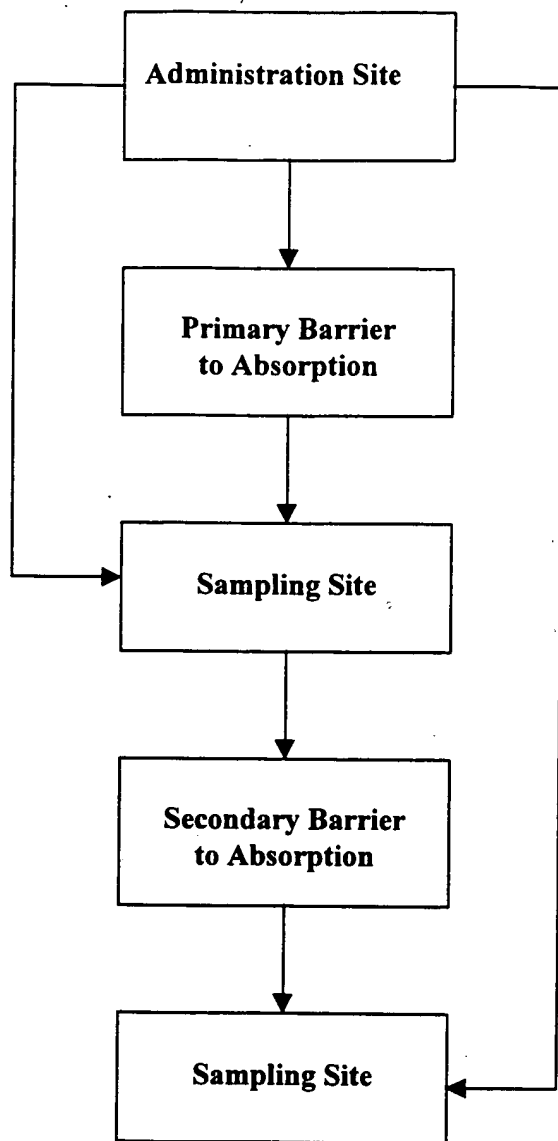


FIG. 2

FIG. 3

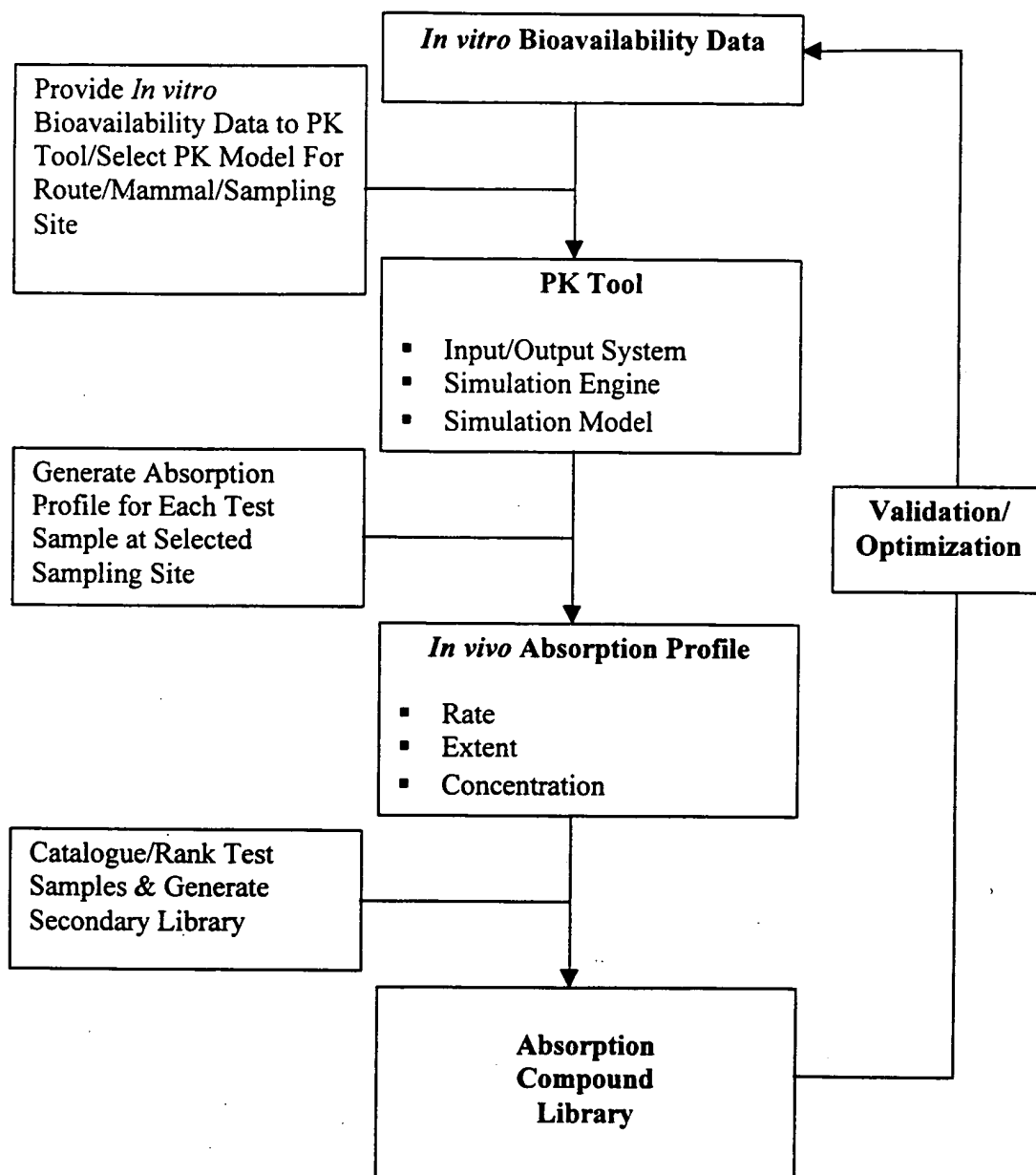


FIG. 3

FIG. 4

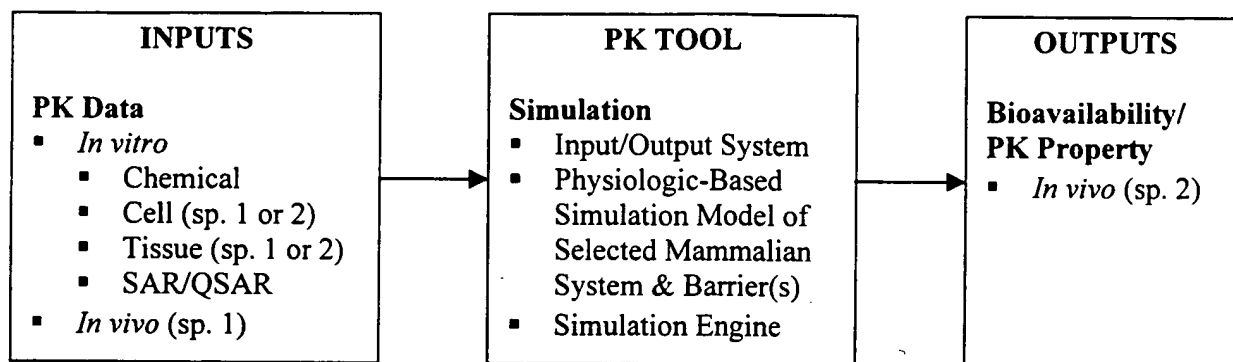


FIG. 5

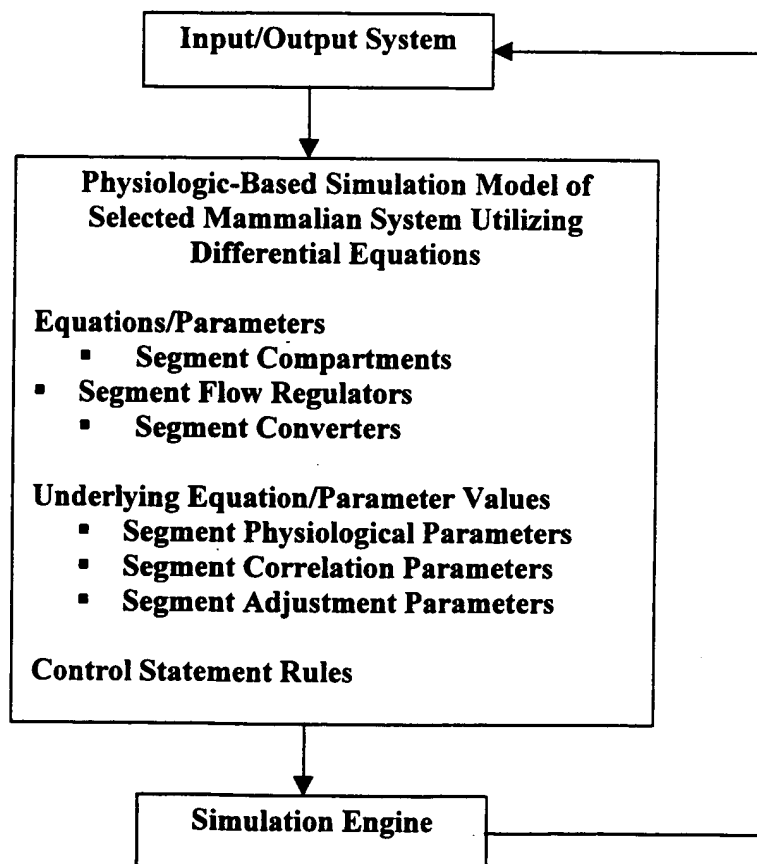


FIG. 4

FIG. 6

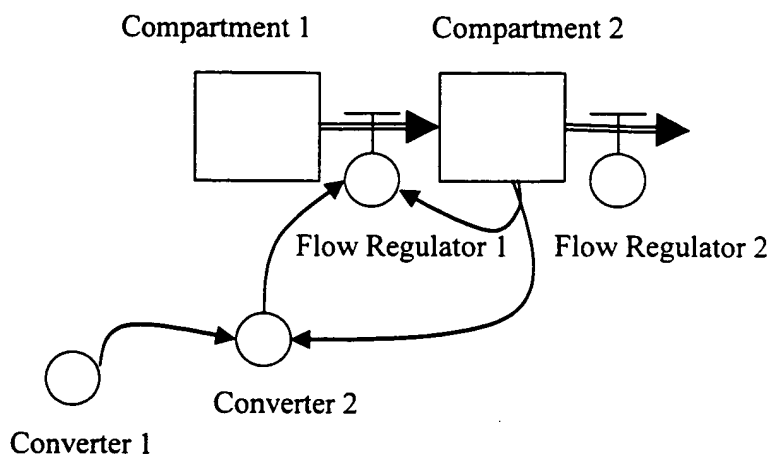


FIG. 7


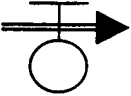


Symbol	Name	Time-Dependent Function
	Compartment	Equation or value for amount of substance stored.
	Flow Regulator	Rate equation for amount of substance transferred.
	Converter	Equation or pre-defined value for (i) input into flow regulator; (ii) input into another converter; and/or (iii) storing value.
	Input Link	Directs input values.

FIG. 8

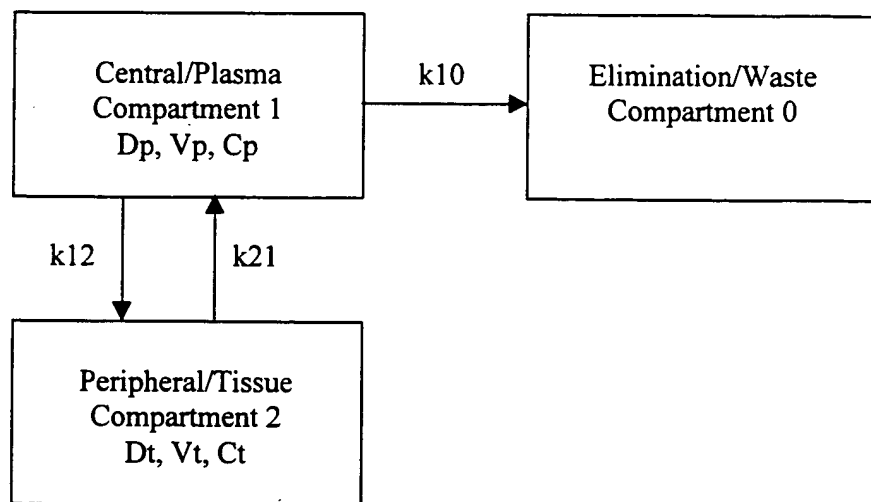


FIG. 9

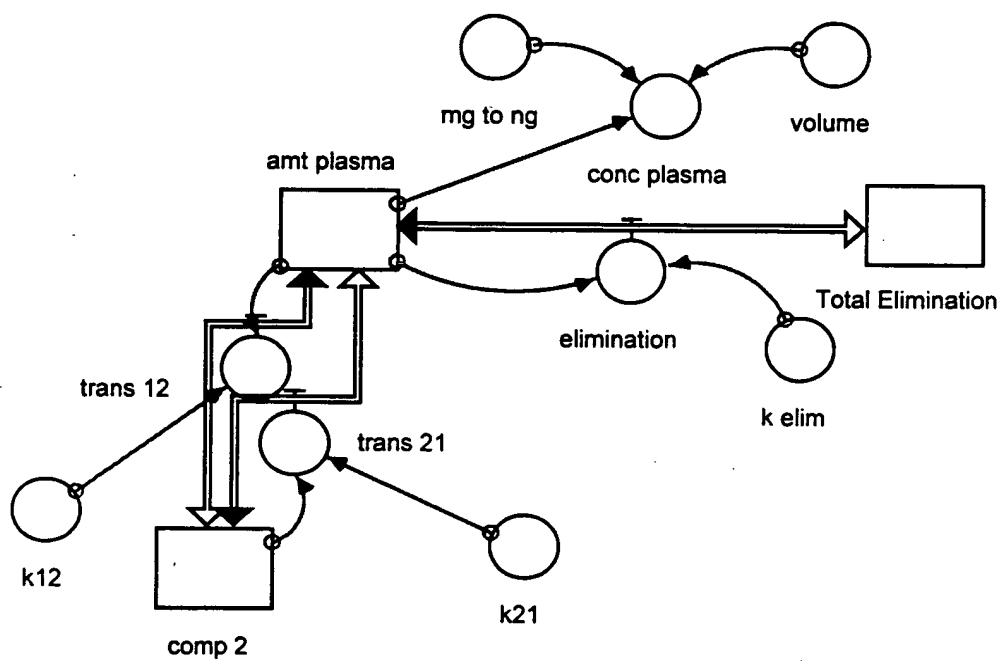


FIG. 10

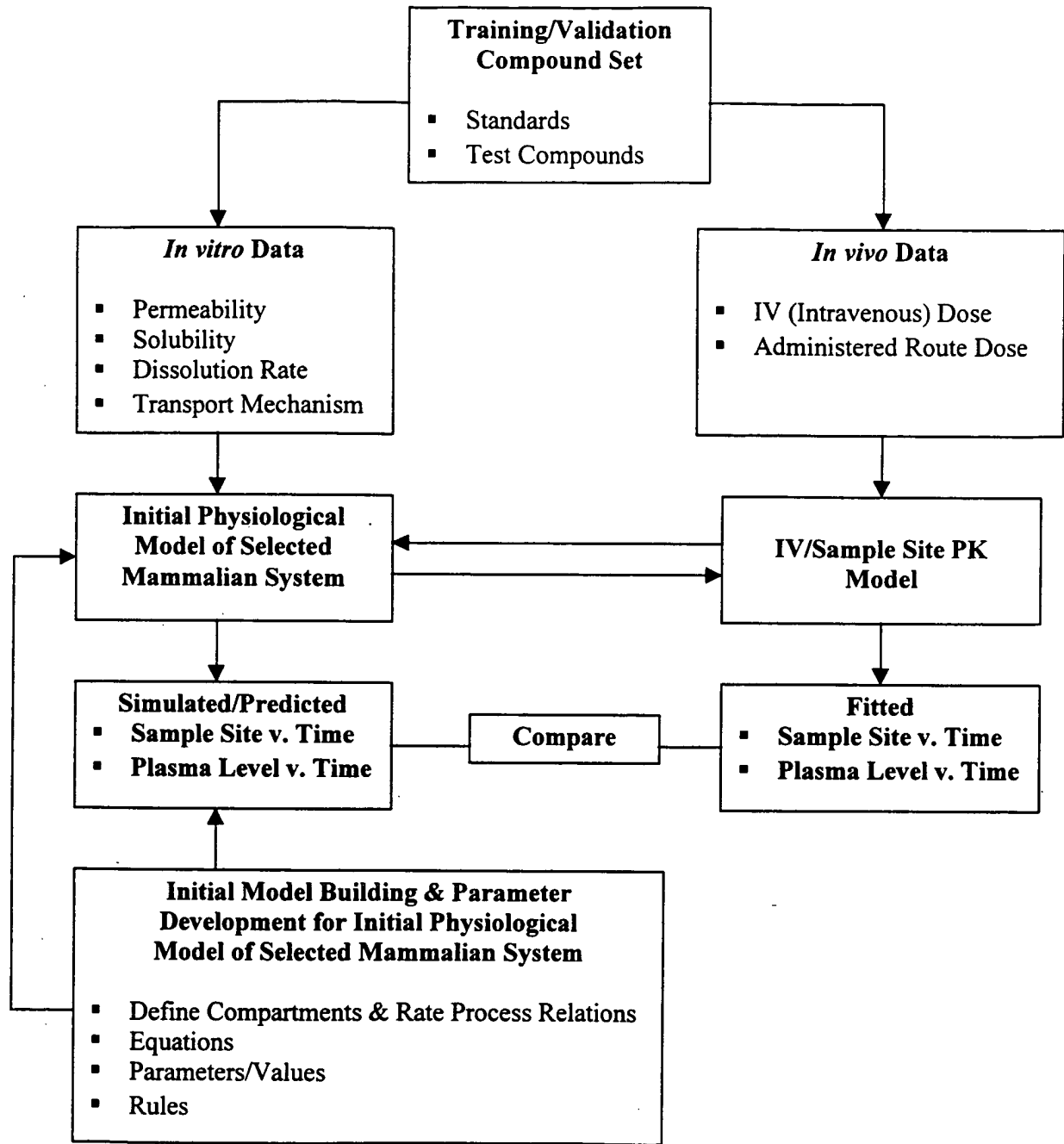


FIG. 10

FIG. 11

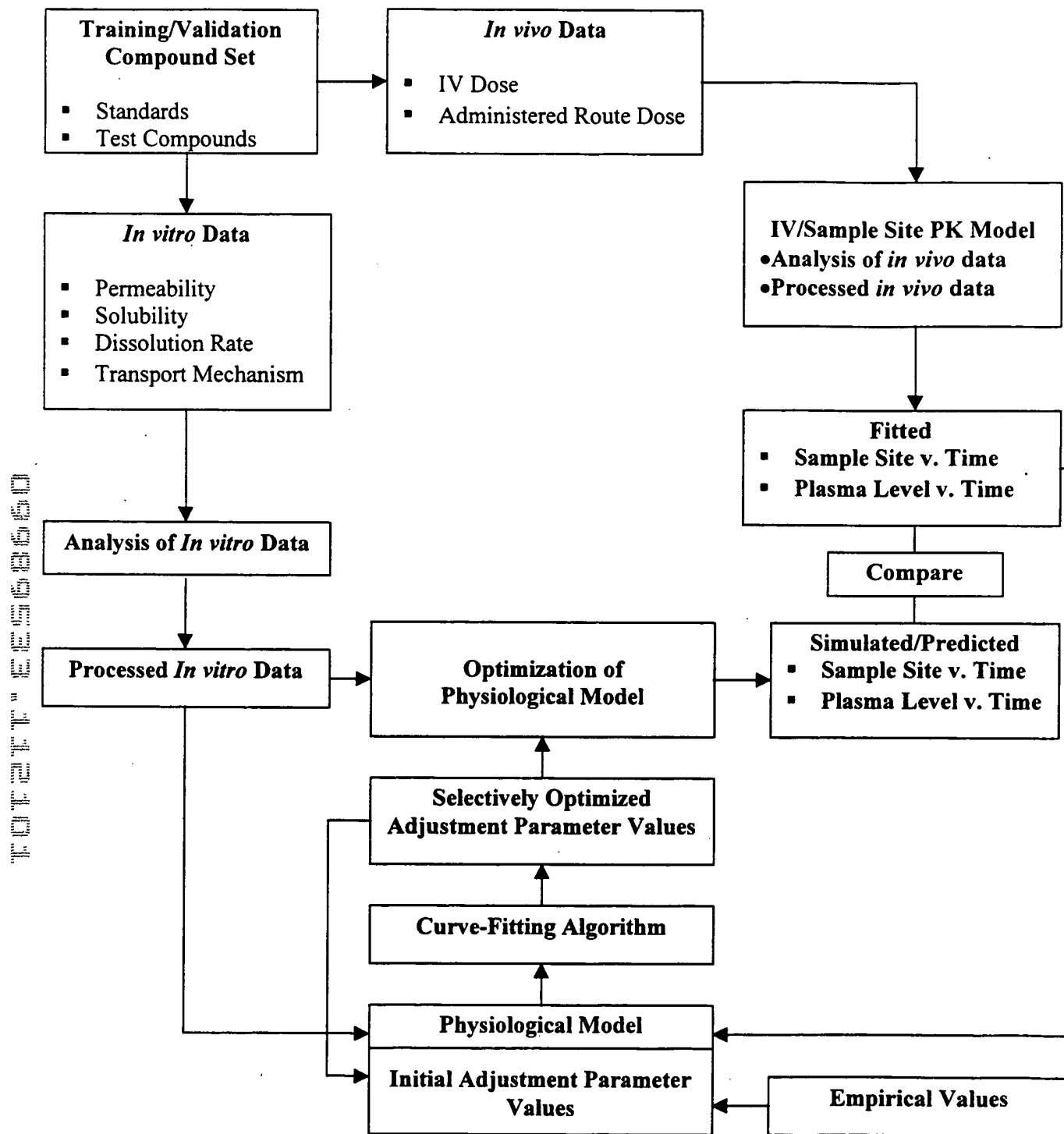


FIG. 12

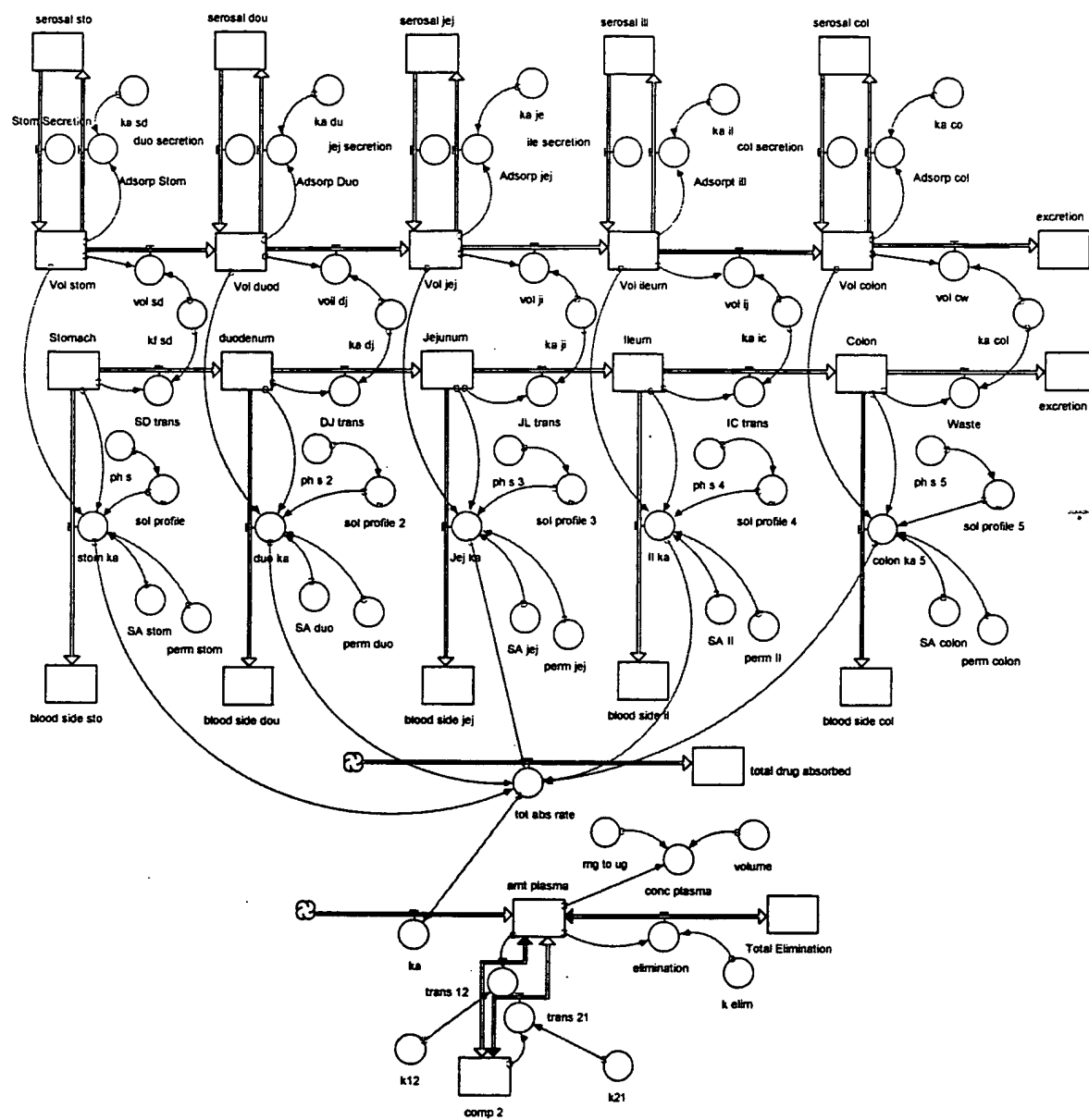


FIG. 13

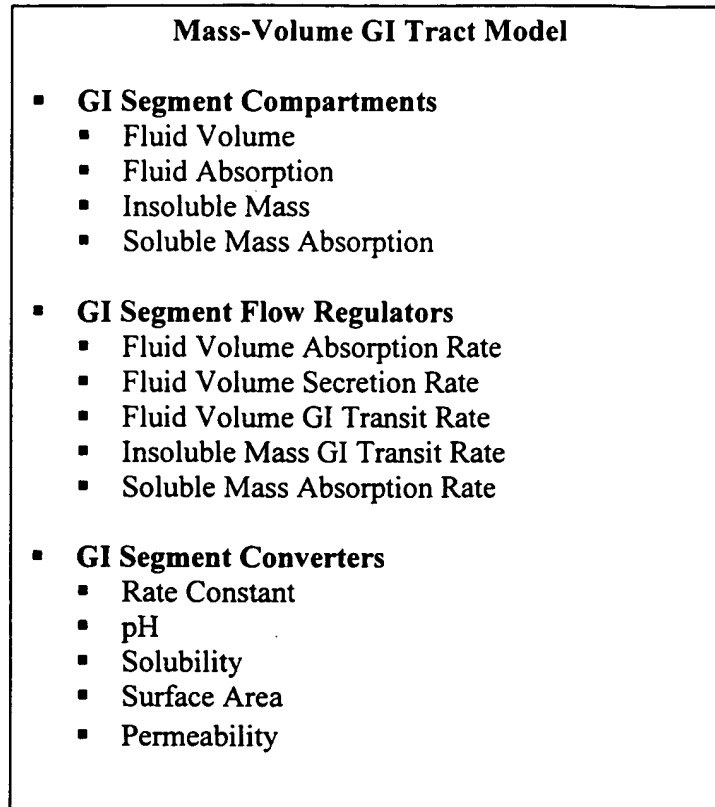


FIG. 14

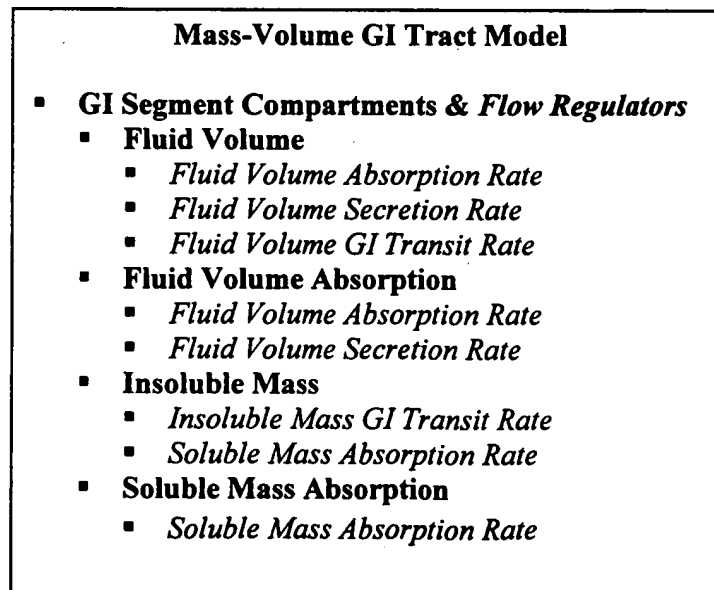


FIG. 15

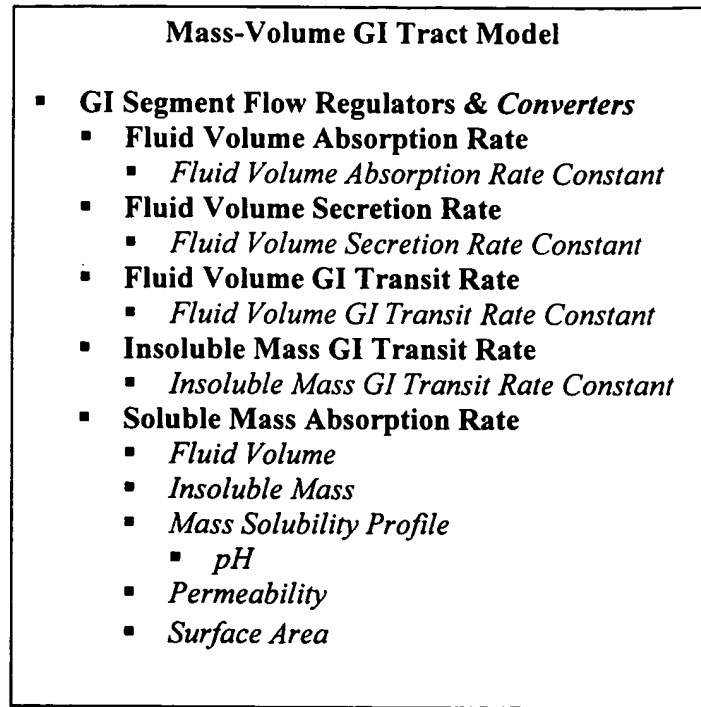


FIG. 16

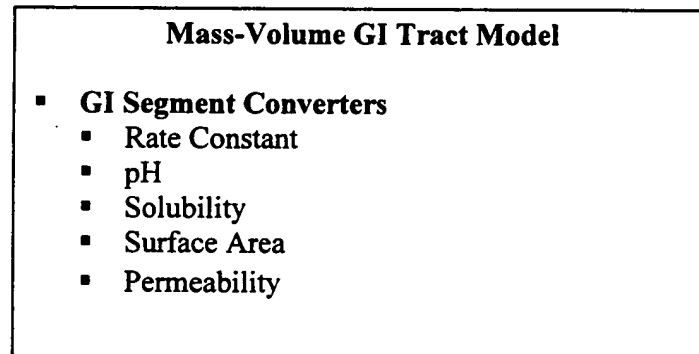


FIG. 17

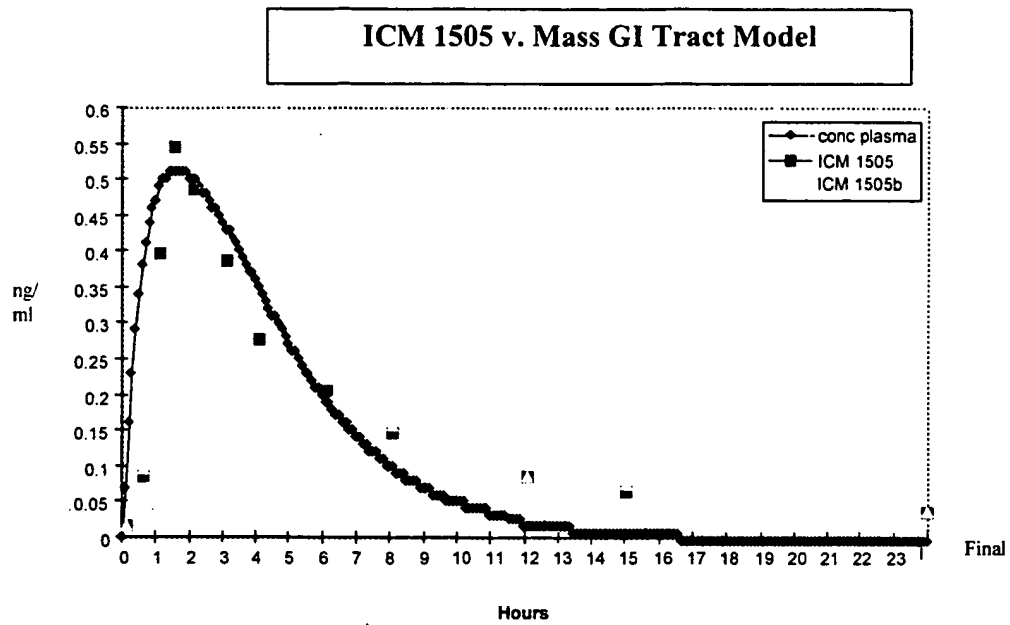


FIG. 18

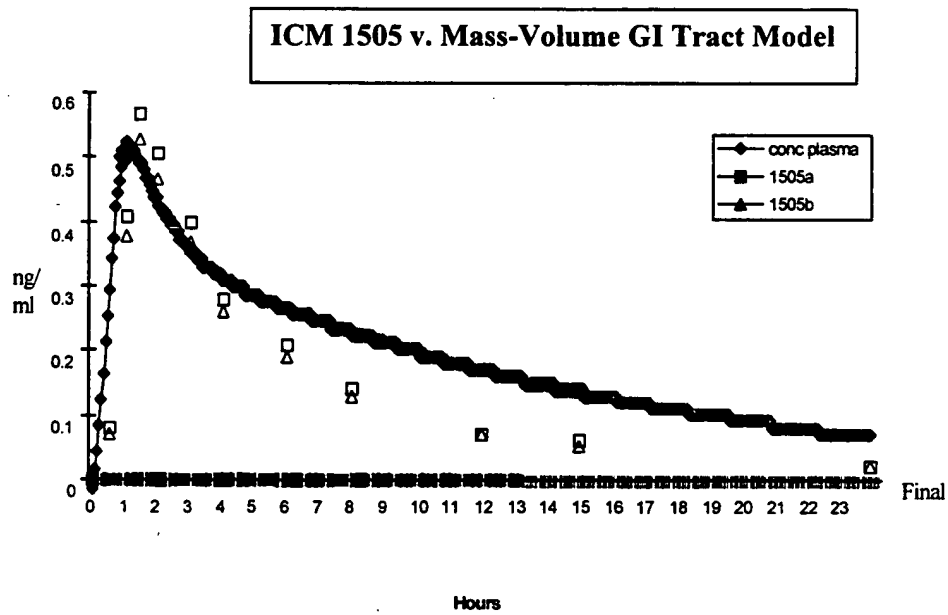


FIG. 19

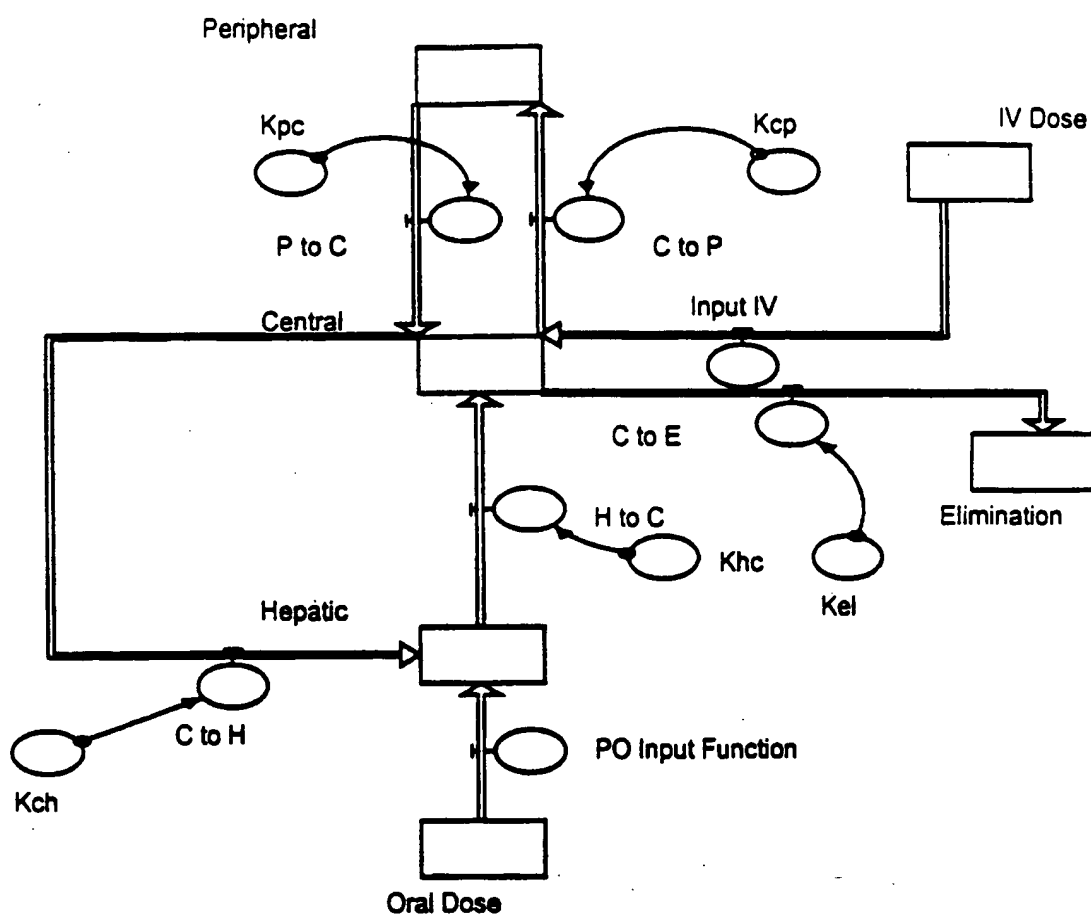


FIG. 20

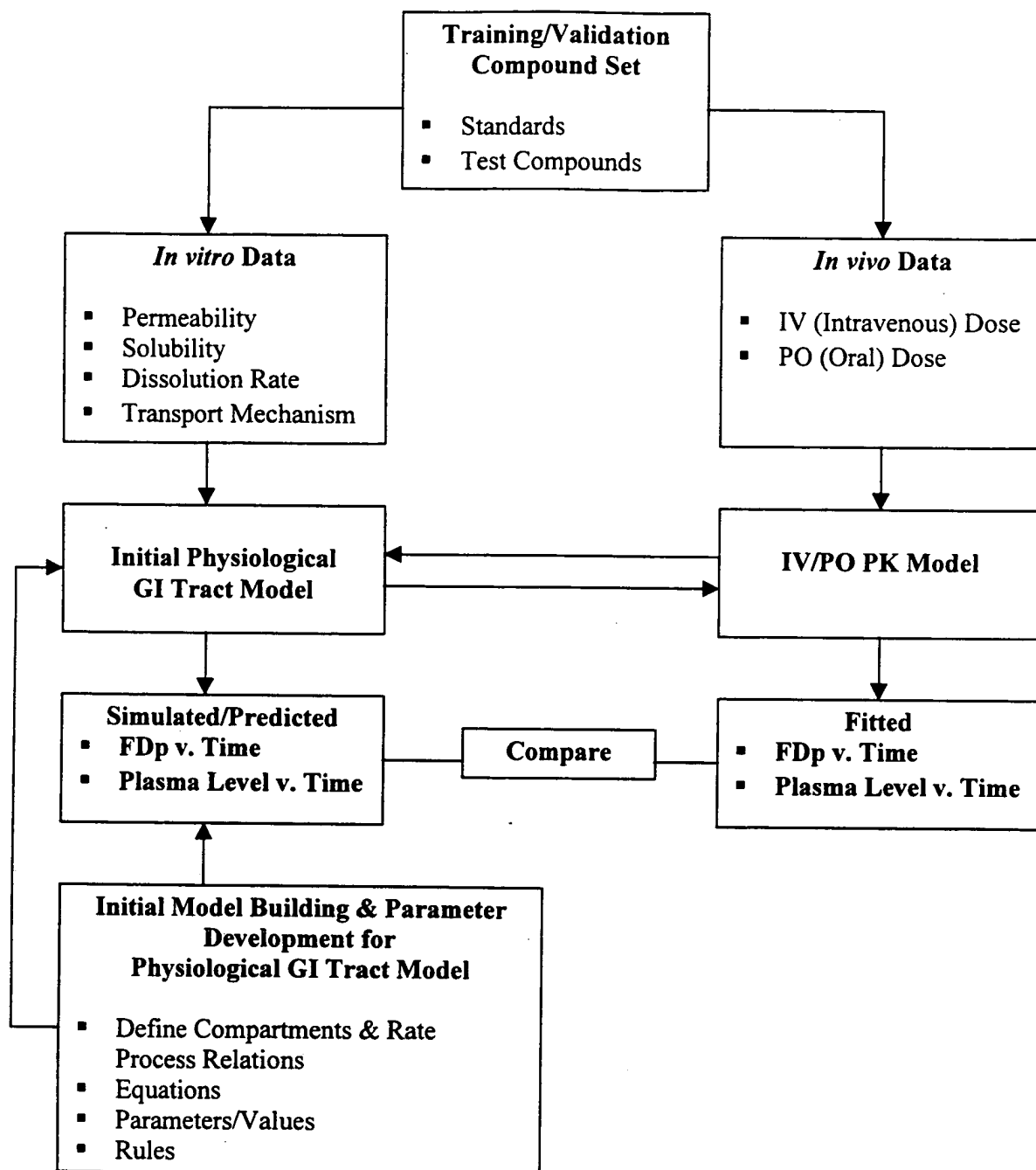


FIG. 20

FIG. 21

Gastrointestinal Transit

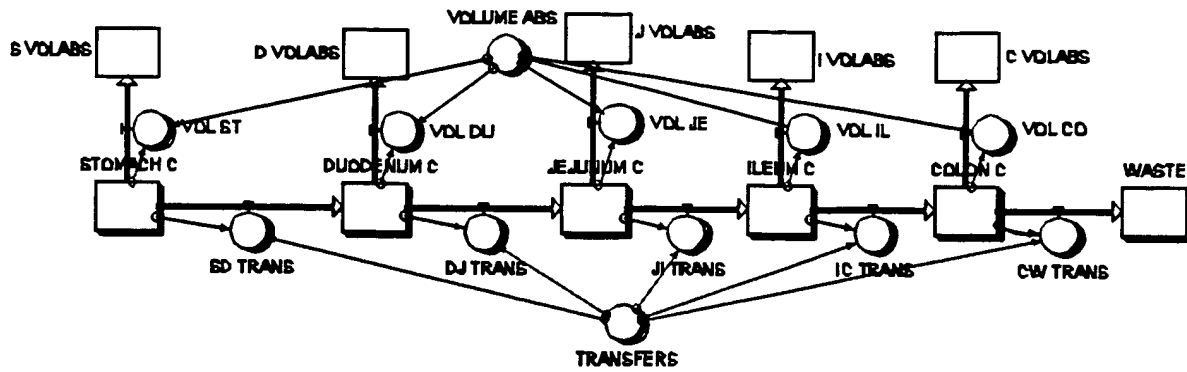


FIG. 22

pH Dependent Solubility and Dissolution

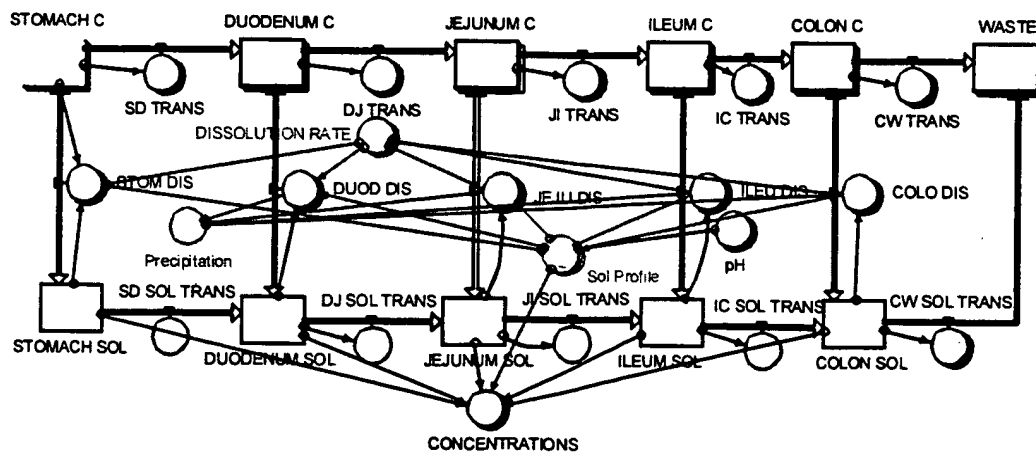


FIG. 23

Absorption

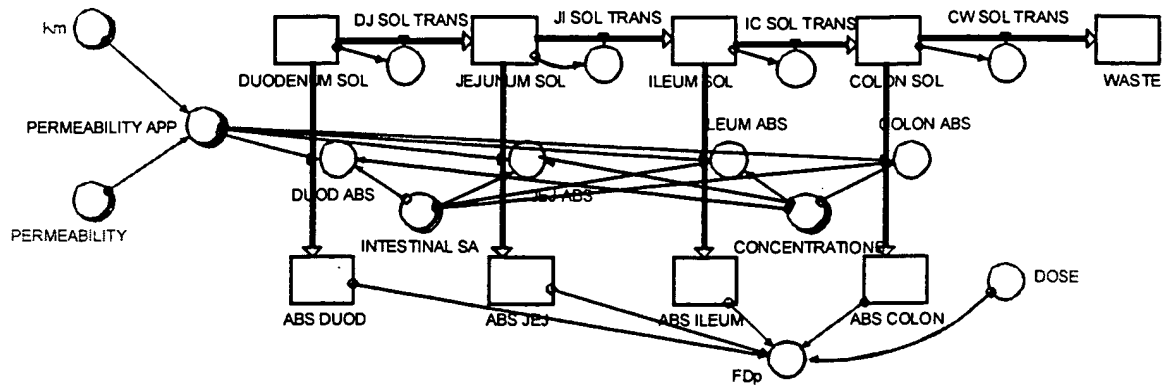


FIG. 24

GI Tract -Intestinal Model

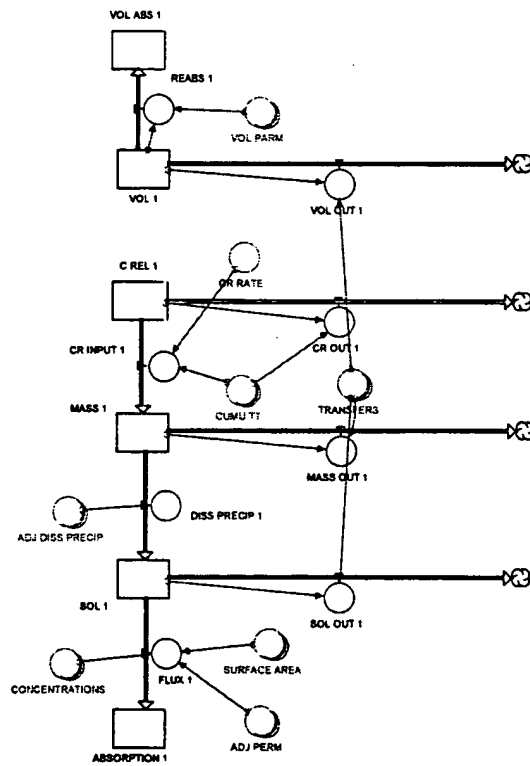
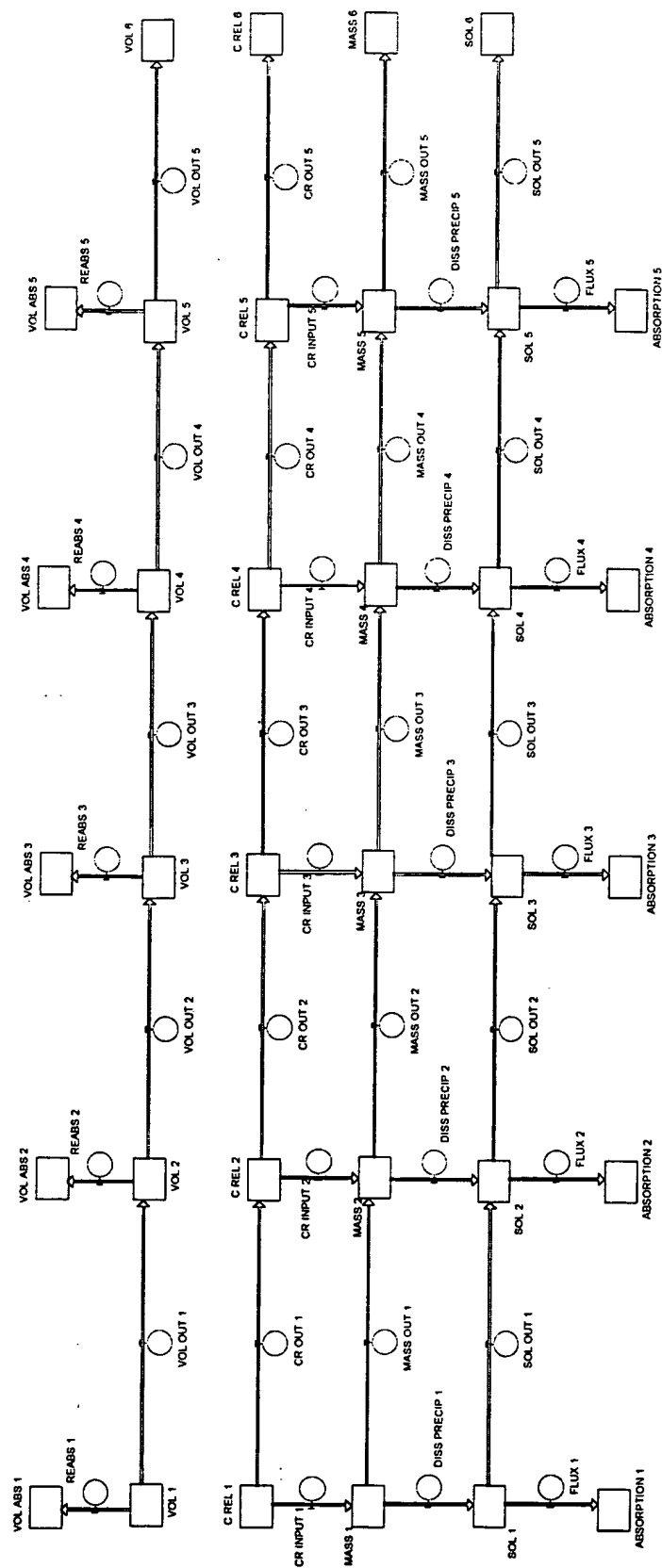


FIG. 25

GI Tract-Intestinal Model (without converters, ghosts or connectors)



GI Tract-Intestinal Model

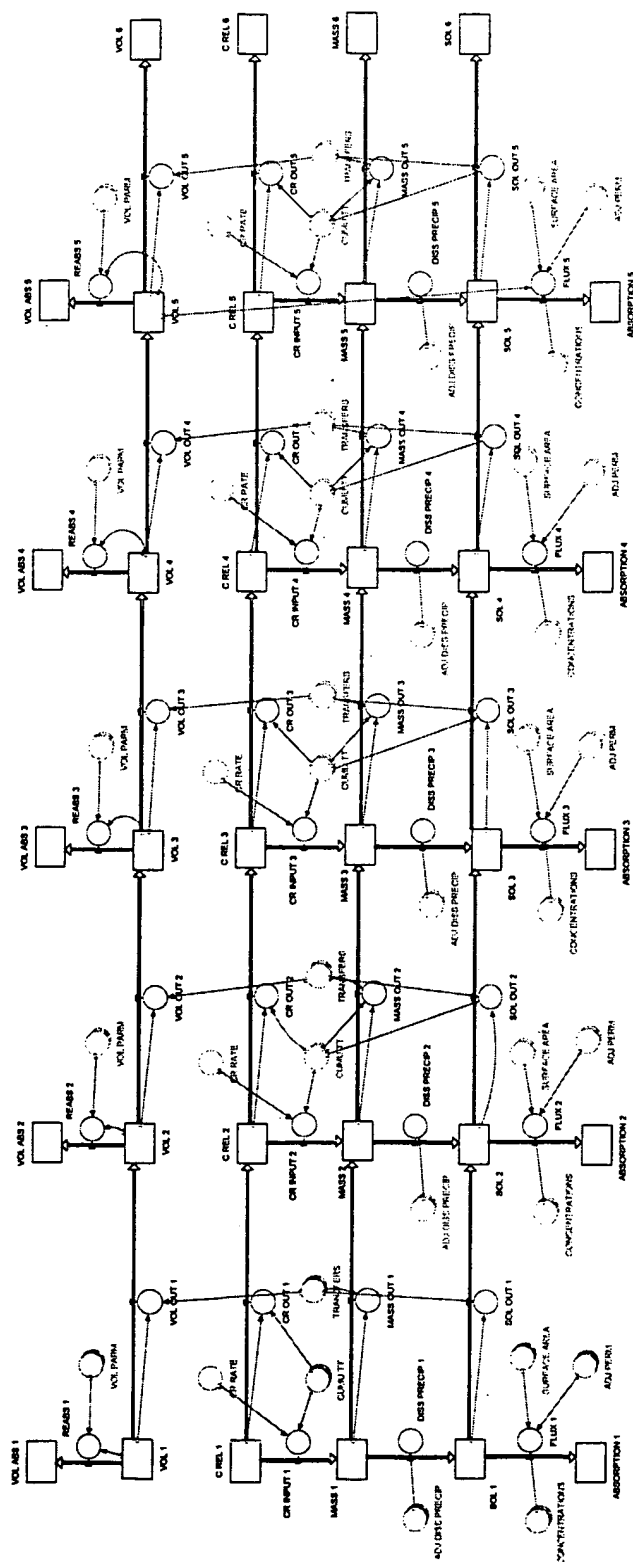


FIG. 27

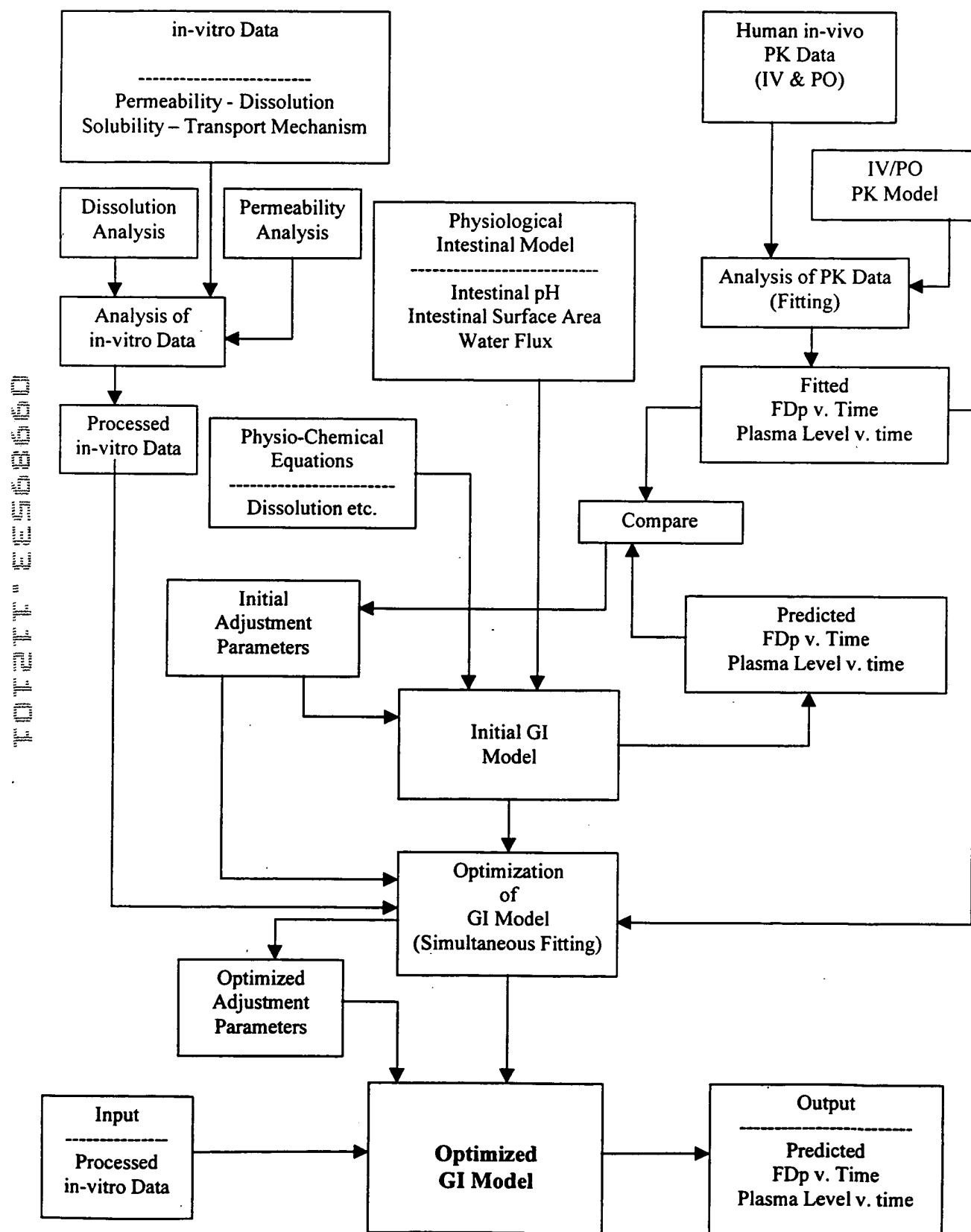


FIG. 28

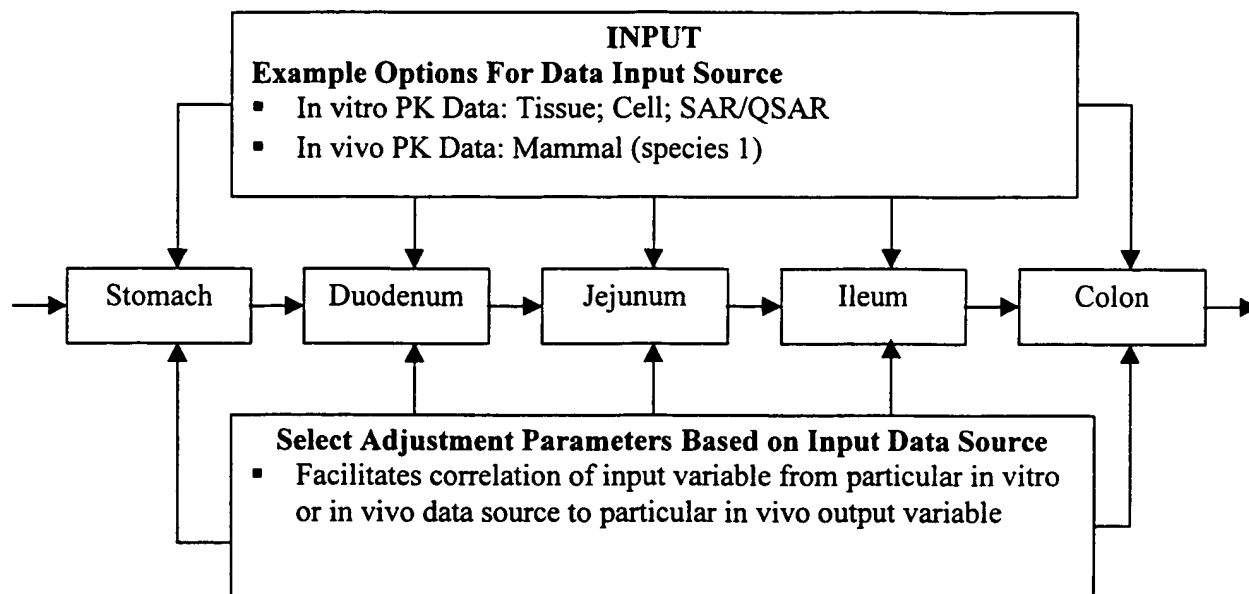


FIG. 29

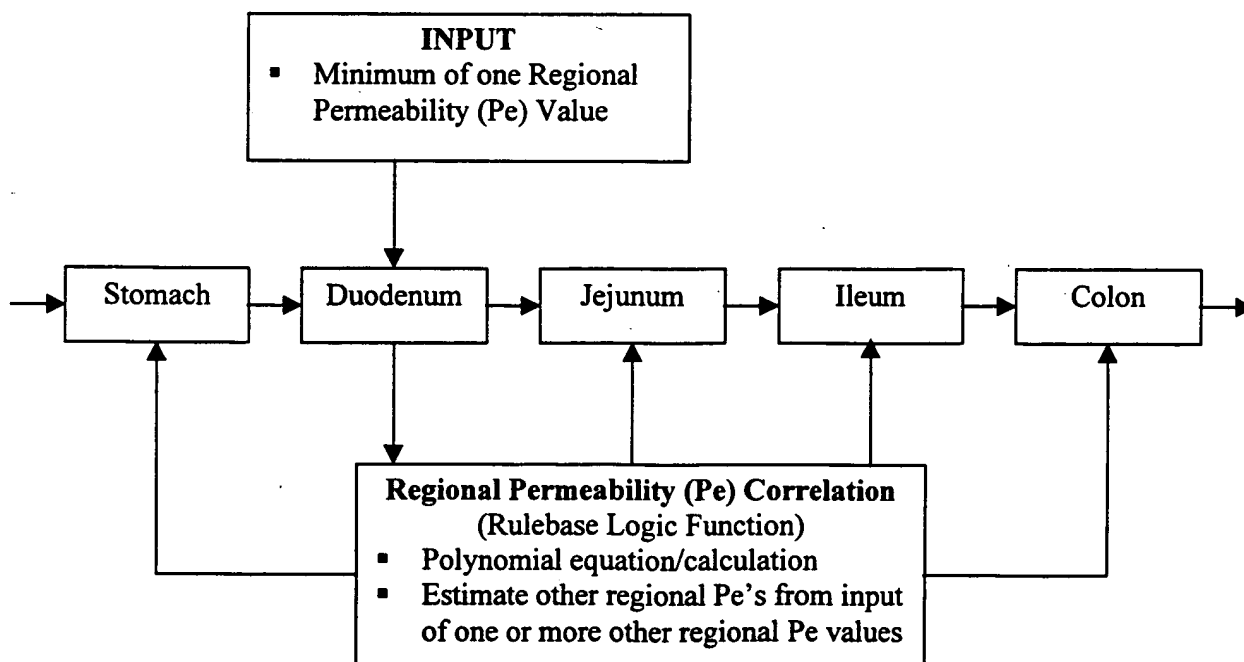


FIG. 30

Parameters

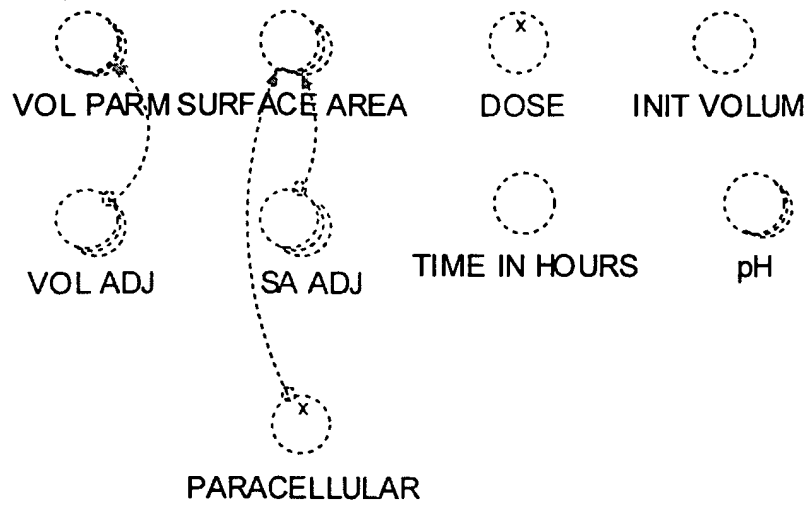


FIG. 31

Transit Time

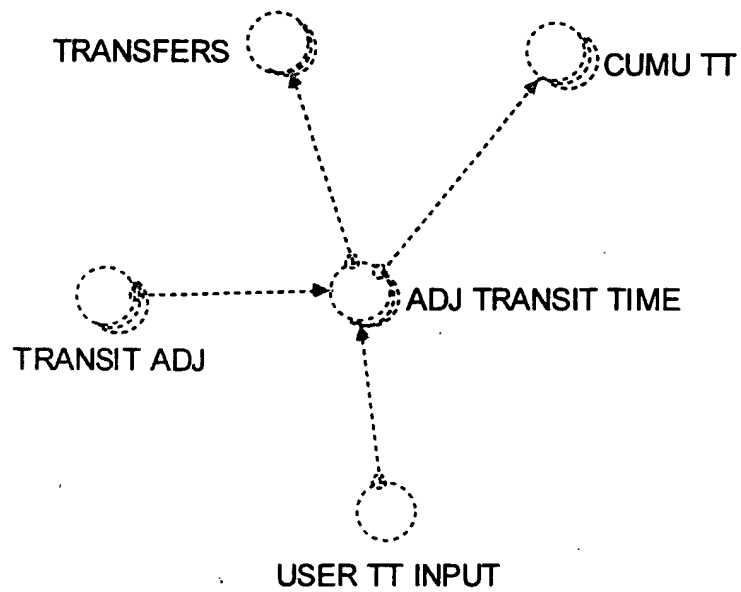


FIG. 30

FIG. 32

Permeability Calculation

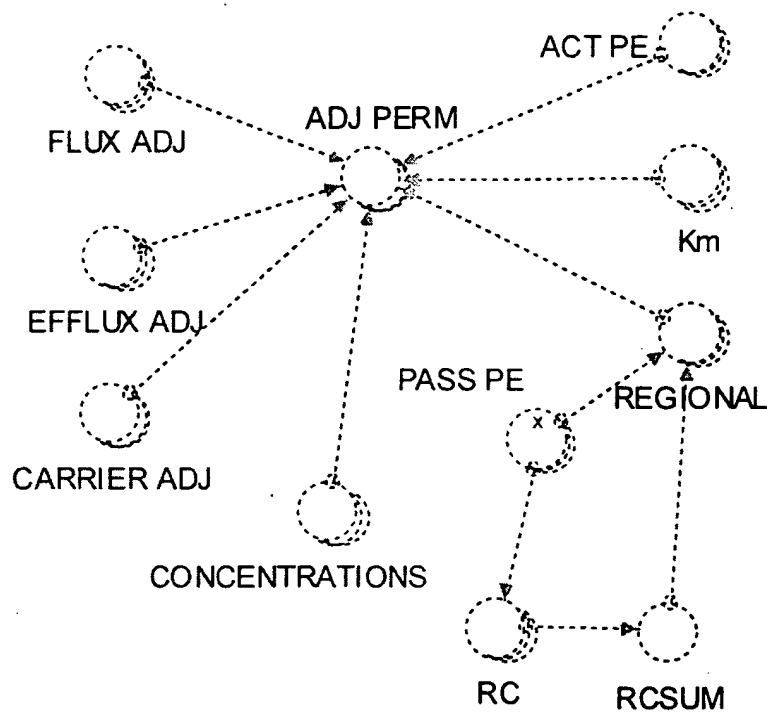
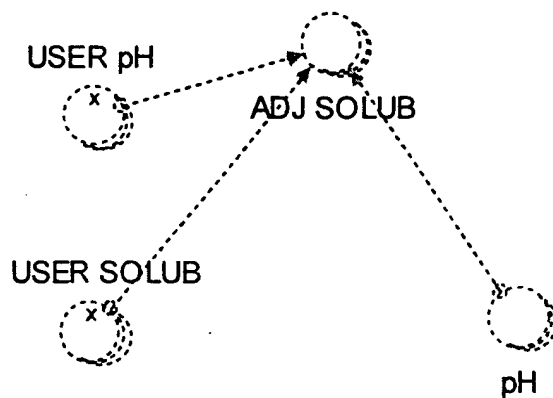


FIG. 33

Solubility Calculation



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FIG. 34

Control Release Calculation

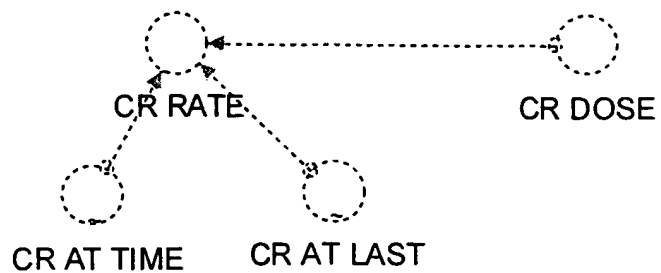


FIG. 35

Concentration Calculation

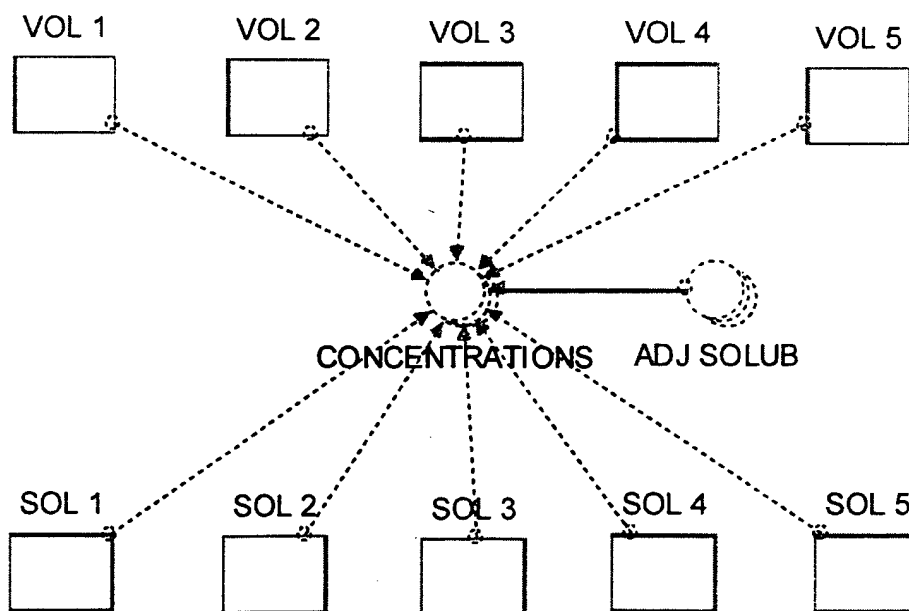


FIG. 34

FIG. 36

Dissolution Calculation

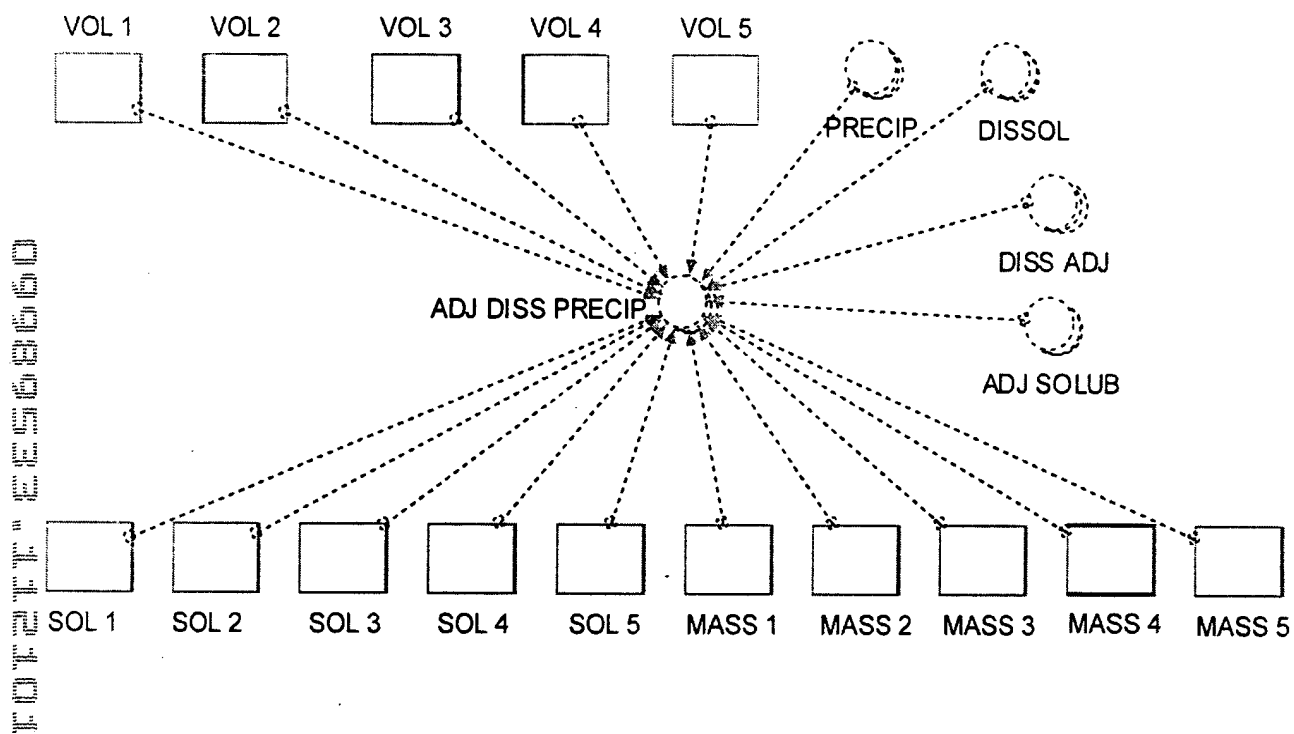


FIG. 37

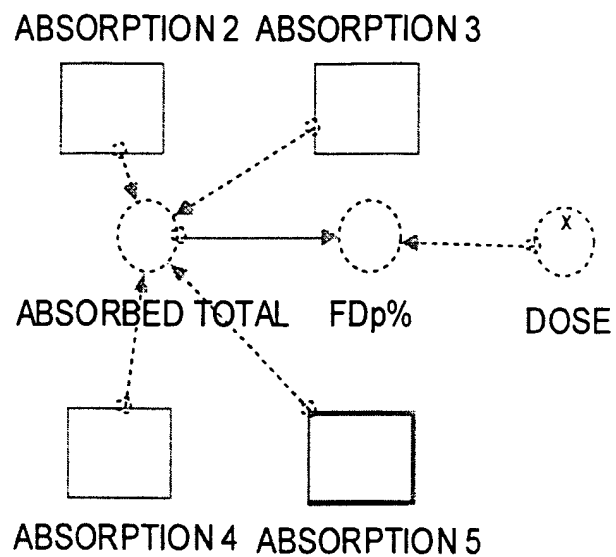


FIG. 38

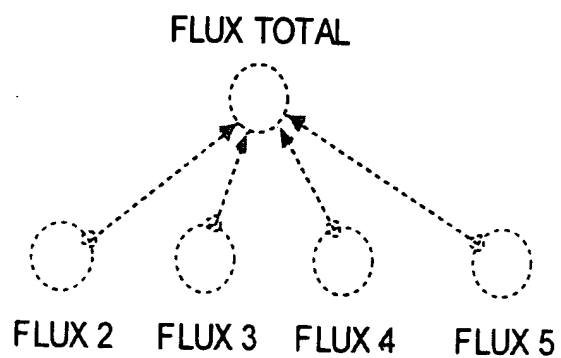


FIG. 39

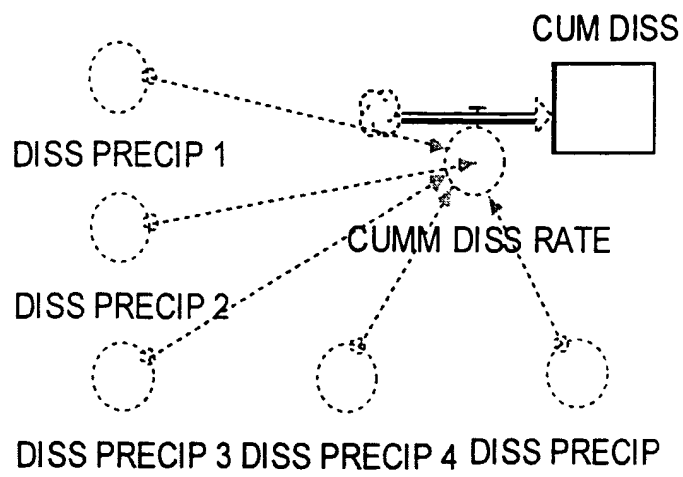


FIG. 40

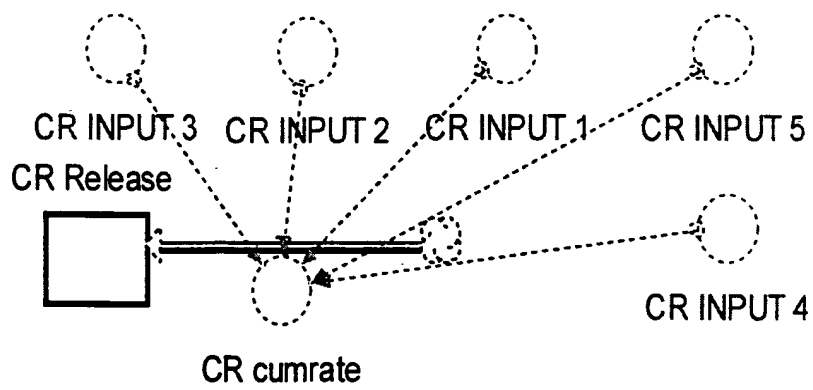


FIG. 41

Physiological GI Tract Model

Database

- **GI Segment Compartments**
 - Fluid Absorption
 - Fluid Volume
 - Insoluble Mass
 - Soluble Mass
 - Soluble Mass Absorption
 - Dosage Form Mass
- **GI Segment Flow Regulators**
 - Fluid Absorption Rate
 - Fluid Volume Transit Rate
 - Insoluble Mass Transit Rate
 - Insoluble Mass Dissolution Rate
 - Soluble Mass Transit Rate
 - Soluble Mass Absorption Rate
 - Dosage Form Disintegration/Release Rate
- **GI Segment Converters**
 - Fluid Volume Absorption Rate Constant
 - GI Transit Rate Constant
 - Adjusted Dissolution Rate Constant
 - Dissolved Drug Concentration
 - Adjusted Surface Area
 - Adjusted Permeability

Rulebase

- GI Transit
- Dissolution
- Absorption
- Permeability Calculations
- Concentration Calculations
- Computational Error Corrections

FIG. 41

FIG. 42

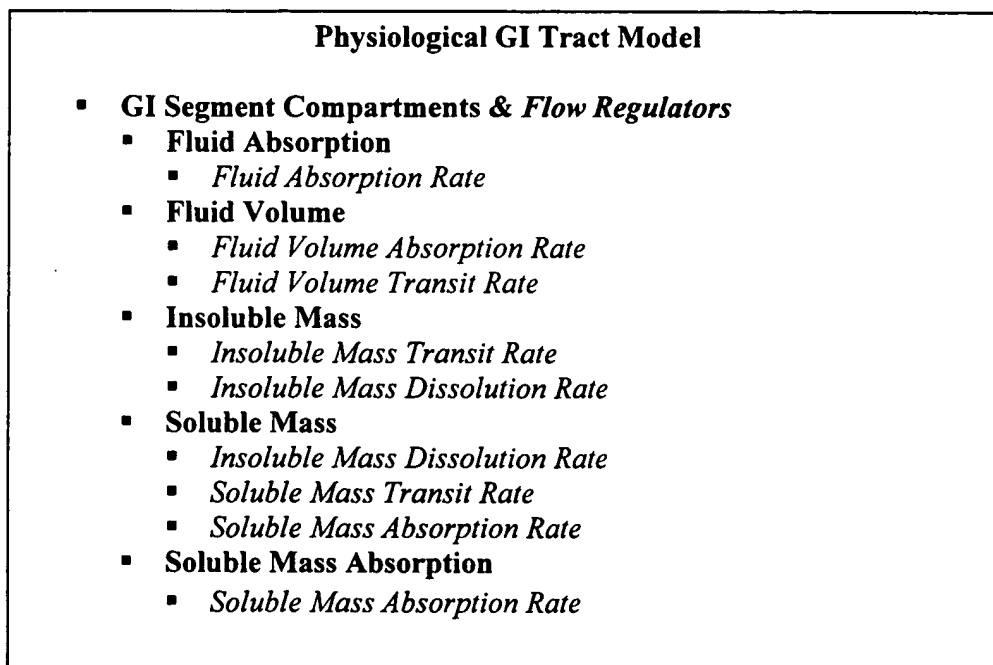


FIG. 43

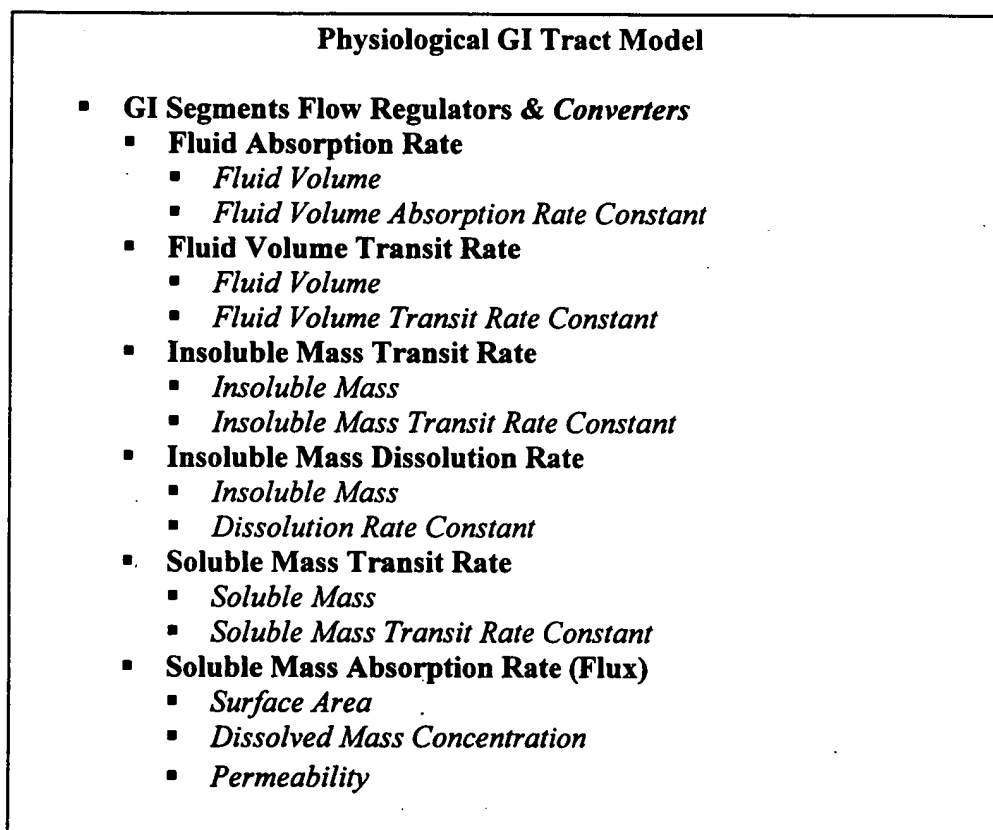


FIG. 44

Physiological GI Tract Model

- **Converters**
 - Permeability
 - Passive Absorption Adjustment Parameter
 - Efflux/Secretion Adjustment Parameter
 - Active Absorption Adjustment Parameter
 - Active or Carrier Mediated Absorptive Permeability
 - Km
 - Passive Permeability/Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Dissolved Mass Concentrations
 - Dissolved Mass Concentration
 - Fluid Volume
 - Solubility
 - pH
 - Solubility
 - Dissolution Rate Constant
 - Fluid Volume
 - Precipitation Rate Constant
 - Dissolution Rate Adjustment Parameter
 - Solubility
 - Insoluble Mass
 - Soluble Mass
 - Surface Area
 - Surface Area Adjustment Parameter
 - Transport Mechanism
 - Transit Rate
 - Transit Time Adjustment Parameter
 - User Adjusted Transit Time
 - Fluid Volume Absorption Rate Constant
 - Fluid Volume Adjustment Parameter

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FIG. 45

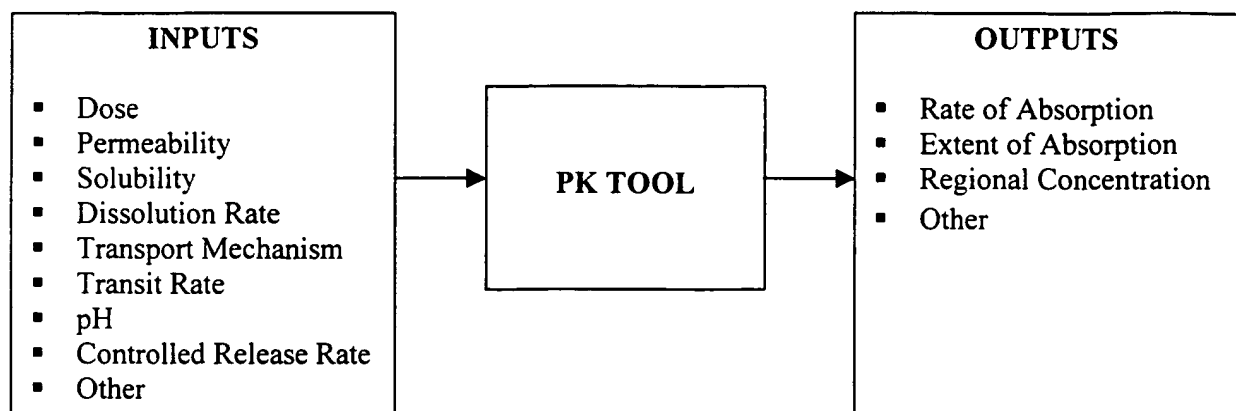


FIG. 46

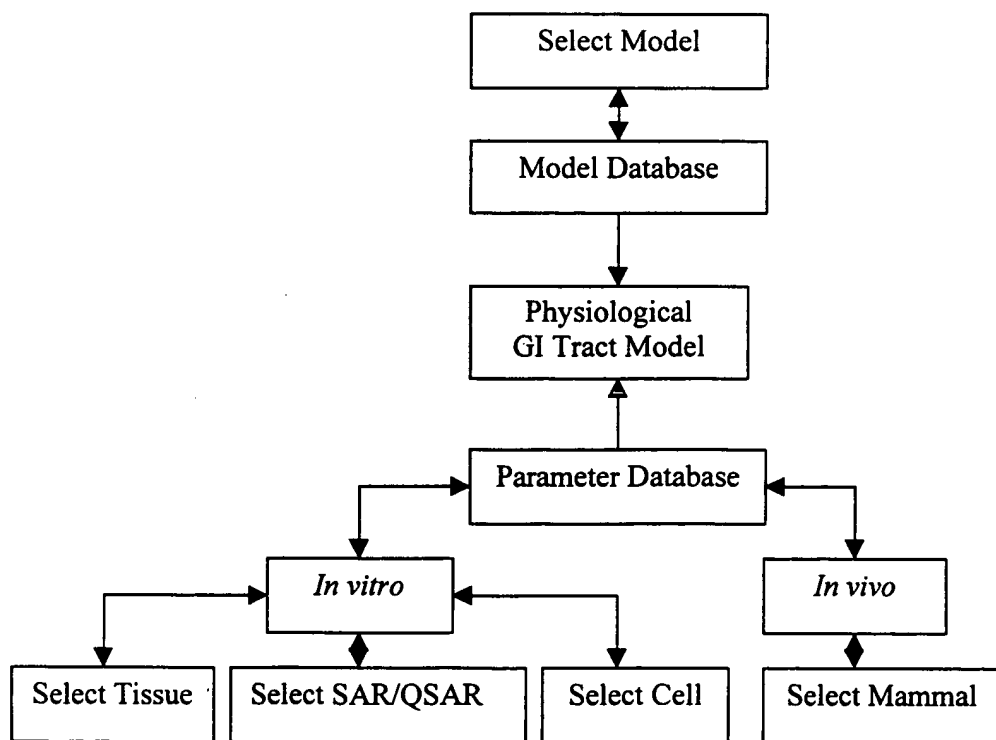


FIG. 47

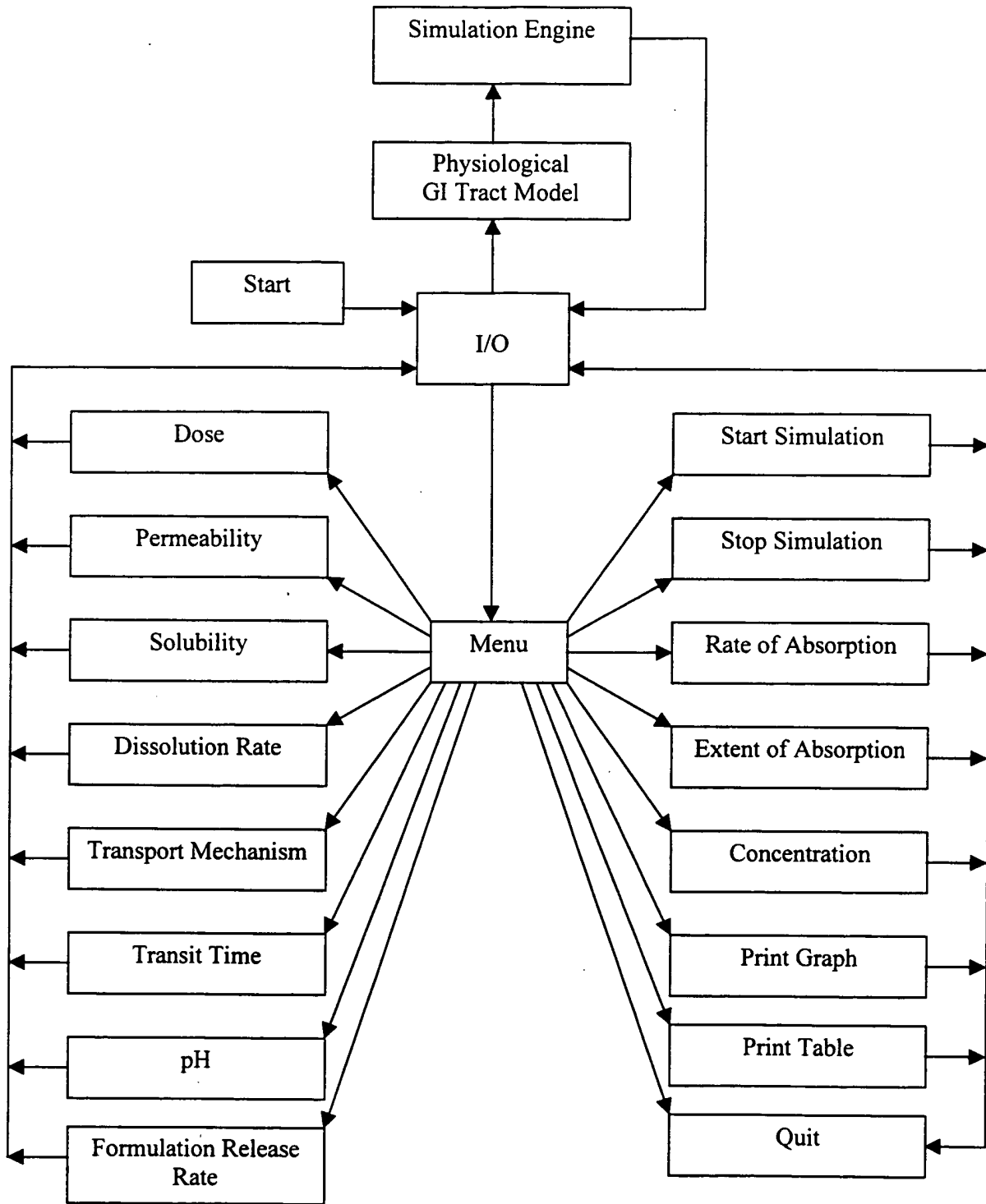


FIG. 47 "EE58550"

FIG. 48

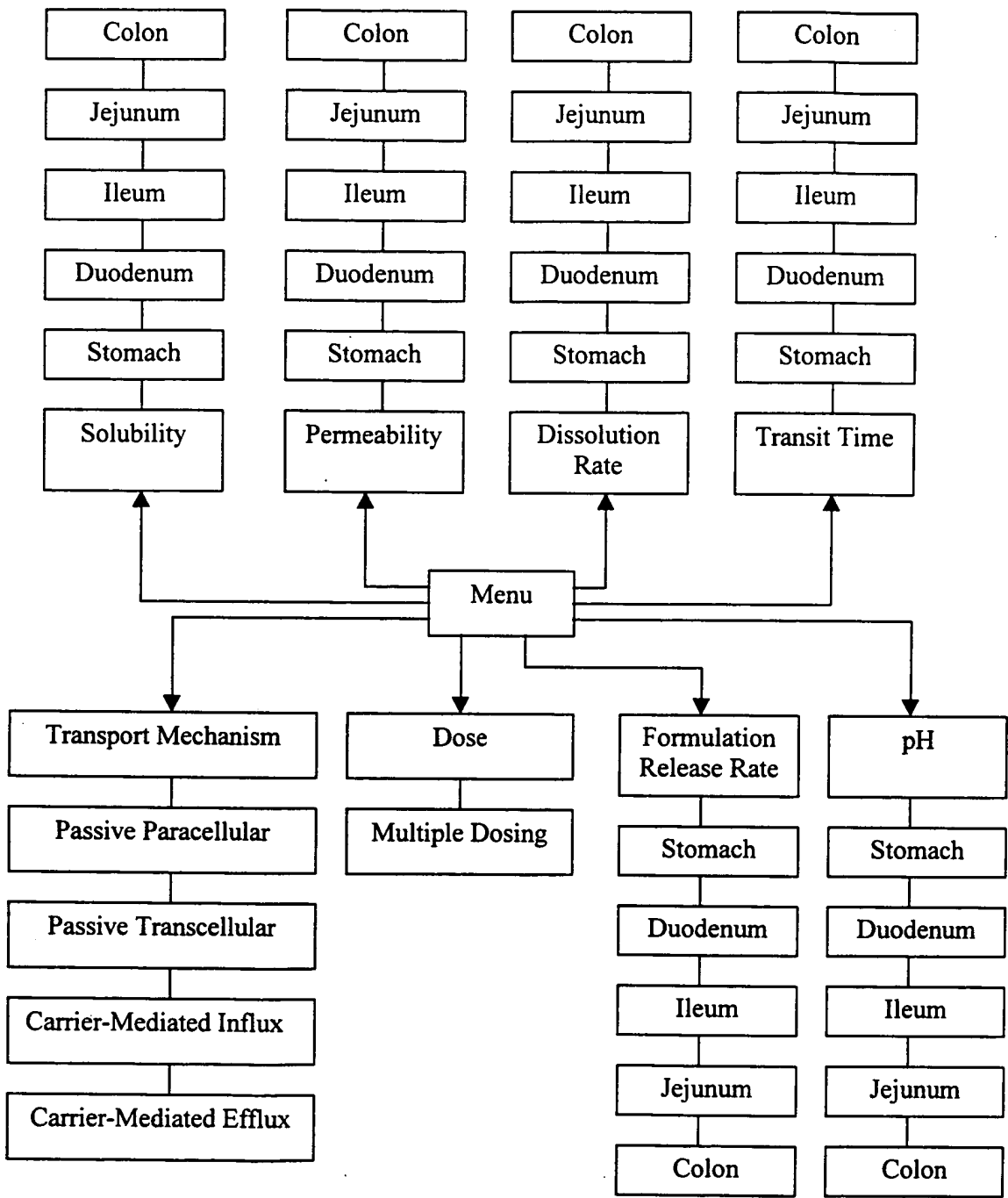


FIG. 48

FIG. 49

Correlation of FDp Extent - GI Model and Pharmacokinetic data

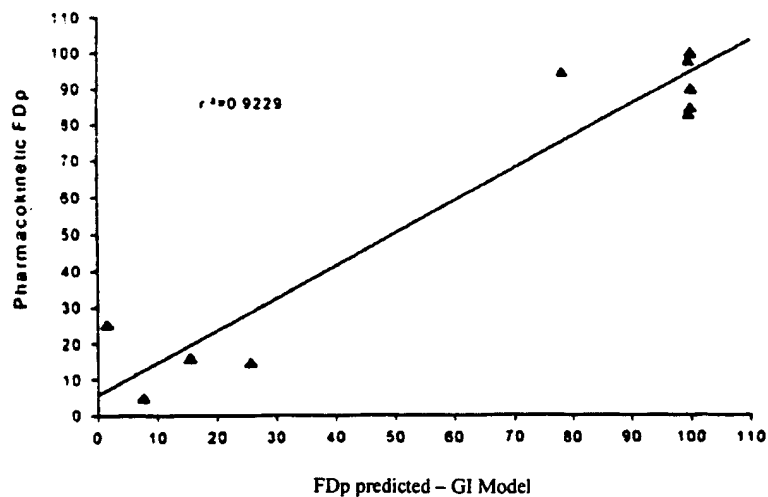


FIG. 50

Correlation of FDp rate of absorption - GI Model and Pharmacokinetic Data

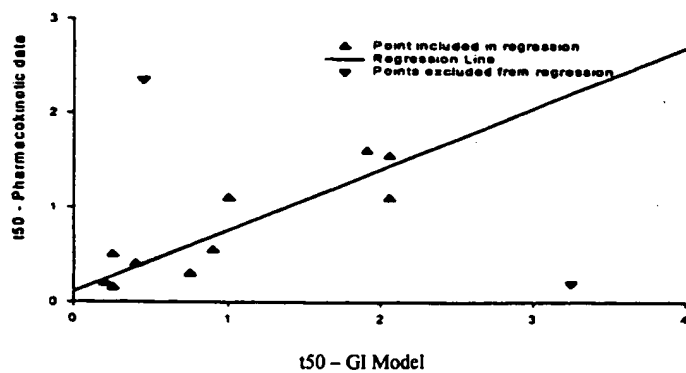


FIG. 51

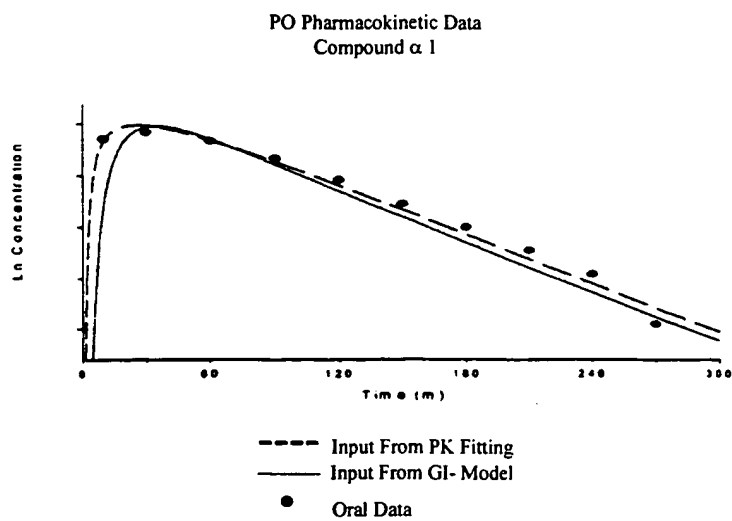


FIG. 52

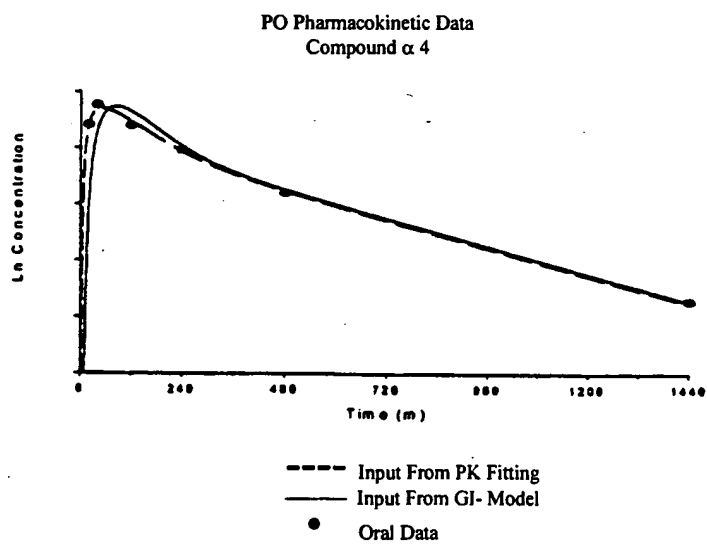
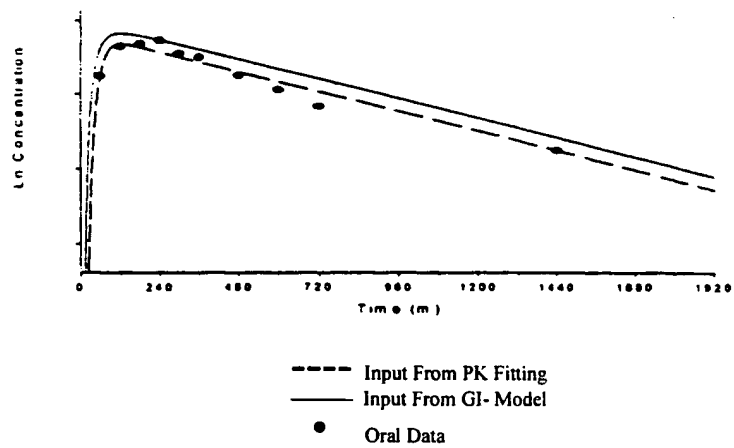


FIG. 53

PO Pharmacokinetic Data
Compound β 6



FOR "E5650"

FIG. 54

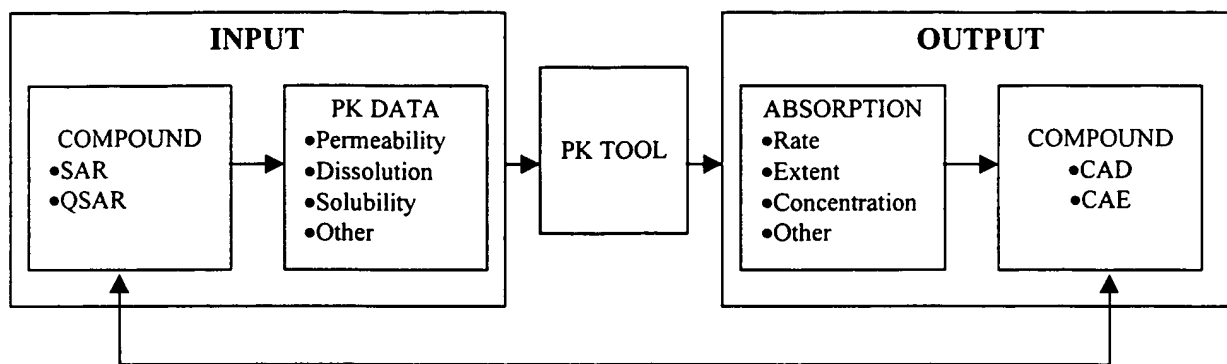


FIG. 55

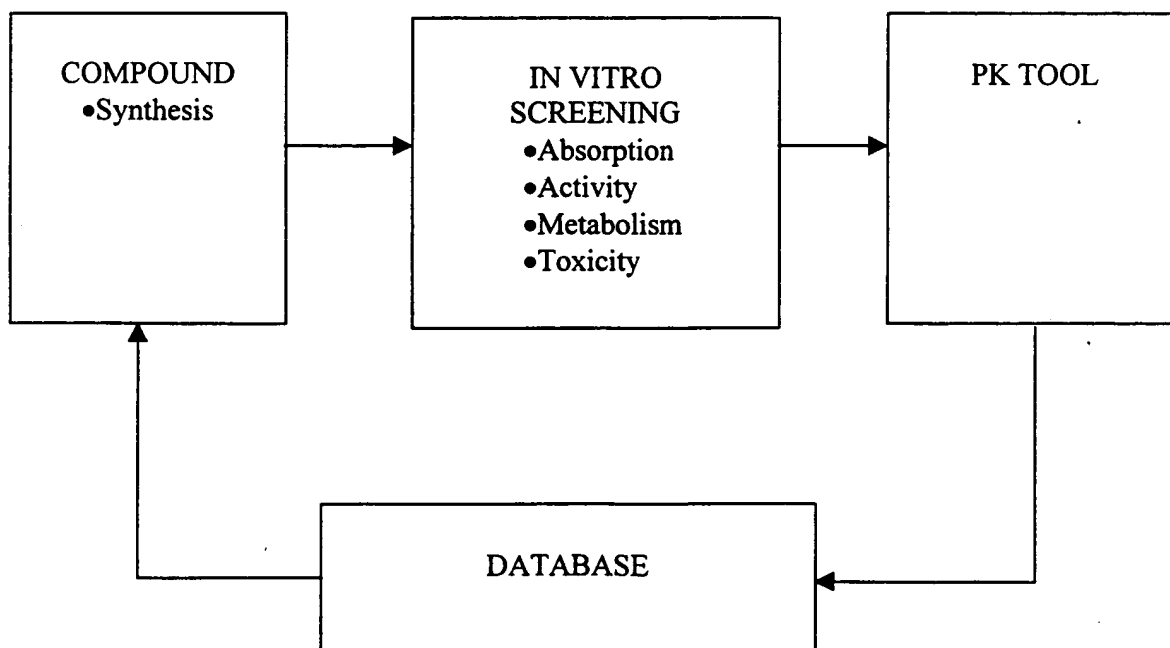


FIG. 54